

Attorney Docket No.: ISPH-0463  
Inventors: Monia et al.  
Serial No.: 09/575,554  
Filing Date: May 22, 2000  
Page 2

#### REMARKS

Claims 1 and 7-20 are pending in the instant application. Claims 1 and 7-20 have been rejected. Reconsideration is respectfully requested in light of the following remarks.

##### I. Double Patenting Rejection

Claim 6 has been rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 1 of U.S. Patent 5,872,242. Applicants respectfully point out that claim 6 was canceled in the previous reply and according to the Examiner's Office Action Summary attached to the present Office Action is not pending in the case. Accordingly, withdrawal of this rejection is respectfully requested as it refers to a claim that has been canceled and is no longer pending.

##### II. Obviousness-Type Double Patenting

Claims 1, 2, 5 and 7-23 have been rejected under the judicially created doctrine of obviousness-type double patenting as

Attorney Docket No.: ISPH-0463  
Inventors: Monia et al.  
Serial No.: 09/575,554  
Filing Date: May 22, 2000  
Page 3

being unpatentable over claims 1-4 of U.S. Patent No. 5,576,208 and claims 1-6 of U.S. Patent No. 5,582,986.

The Examiner suggests that although the conflicting claims are not identical, they are not patentably distinct from each other because the species claims of these patents anticipate the larger genus claims 1, 2, 5 and 7-23 of the current application.

At the outset, Applicants respectfully point out that claims 2, 5 and 21-23 were canceled in the previous reply, and, according to the Examiner's Office Action Summary attached to the present Office Action, are not pending in the case. Accordingly, withdrawal of this rejection with respect to those claims is respectfully requested as it refers to claims that have been canceled and are no longer pending.

With respect to claims 1 and 7-20, which are pending, since the instant invention and the patents cited are commonly owned, a terminal disclaimer in compliance with 37 CFR 1.321 has been filed herewith. Withdrawal of this rejection to the claims is therefore respectfully requested.

### III. Rejection of Claims Under 35 U.S.C. 103(a)

The rejection of claims 1 and 7-20 under 35 U.S.C. 103(a) as being unpatentable over Bos, Daaka et al., Hall et al., and Saison-

Attorney Docket No.: ISPH-0463  
Inventors: Monia et al.  
Serial No.: 09/575,554  
Filing Date: May 22, 2000  
Page 4

Behmoaras et al., each in view of Uhlmann et al, Agrawal et al., and Inoue et al., and further in view of Smith, has been maintained. The Examiner suggests that the invention as a whole was *prima facie* obvious because Bos discloses antisense oligonucleotides to human H-ras and Ki-ras and to specific regions of ras genes that are mutated in the activated forms, because Hall et al. teach the sequence of N-ras from which specific antisense molecules are derived, because Daaka et al. teach antisense molecules to the translation initiation site of H-ras gene and their use to inhibit expression of H-ras, and because Saison-Behmoaras et al. teach oligonucleotide that specifically hybridize to the codon 12 region of H-ras and methods to inhibit gene expression. The teaching of these primary references is suggested by the Examiner to be supplemented by the teaching of modification to antisense oligonucleotides by Uhlmann et al., Agrawal et al., and Inoue et al., while Smith et al. teach use of antisense compounds against oncogenes or genes that are differentially expressed in tumor cells as treatment for cancer. The Examiner goes on to suggest that motivation is provided by Saison-Behmoaras et al., Daaka et al., and Bos et al. Applicants respectfully disagree with the Examiner's conclusions.

Attorney Docket No.: ISPH-0463  
Inventors: Monia et al.  
Serial No.: 09/575,554  
Filing Date: May 22, 2000  
Page 5

Applicants respectfully point out that the claims have been amended to be limited to specific SEQ ID NO's for antisense compounds targeted to Ki-ras. As discussed in the previous reply and as acknowledged by the Examiner at page 10 of the Office Action, none of the primary references, either alone or combined, cited by the Examiner teach antisense compounds with specific sequences that are targeted to Ki-ras. Although Bos et al. teach the sequence of Ki-ras itself, this reference does not teach antisense to Ki-ras. None of the other references teach antisense compounds targeted to Ki-ras. A mere teaching of antisense to another target is not sufficient to enable specific antisense sequences to another different target.

To establish a *prima facie* case of obviousness, three basic criteria must be met. MPEP 2143. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art must teach or suggest all claim limitations. Clearly, the combination of prior art cited fails to teach or suggest the limitations of the claims as amended, which claim specific antisense oligonucleotide sequences targeted to human Ki-

Attorney Docket No.: ISPH-0463  
Inventors: Monia et al.  
Serial No.: 09/575,554  
Filing Date: May 22, 2000  
Page 6

ras, and thus cannot render the instant claimed invention obvious.  
Withdrawal of this rejection is therefore respectfully requested.

#### IV. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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